

## **REMARKS**

Claims 1-22, 24-25, 27-95, 97-98, and 100-147 are pending. Claims 1 and 74 are amended. No new matter is added.

### **Claim Objections**

The Office Action states that claims 1-22, 24-25, 27, 67-95, 97-98, 100, and 140-147 are objected to because they recite the term N-acetyl-beta-D-glucosamine twice. Applicants thank the Examiner for calling their attention to the inadvertent repetition of the word "N-acetyl-beta-D-glucosamine" in the claims. The claims are being herewith amended solely in order to correct these informalities.

### **Rejection of Claims 1, 4-12, 69-70, 72-74, 77-85, 142, 144, and 146 Under 35 U.S.C. §102(b)**

The Office Action states that claims 1, 4-12, 69-70, 72-74, 77-85, 142, 144, and 146 are rejected under §102(b) as anticipated by Ramshaw et al. This rejection, with respect to then pending claims 1-2, 4-8, 15-16, 18-21, 69-70, 72-75, 77-81, 88-89, 91-94, 142, 144, and 146, was made previously in the non-final office action mailed on October 5, 2005. Applicants' arguments made in the response filed April 5, 2006 were apparently sufficient to overcome the rejection since the rejection was not maintained in the Final Office Action mailed July 12, 2006. Applicants are, therefore, uncertain as to the grounds for the re-assertion of a rejection that was already overcome. Nevertheless, because the rejection has been re-asserted, Applicants provide the following remarks to distinguish the instant invention over the teachings of Ramshaw et al.

The Office Action rejects claims 1, 4-12, 69-70, 72-74, 77-85, 142, 144, and 146 under §102 for lack of novelty over Ramshaw et al., U.S. Pat. No. 5,866,131. The Office Action asserts that Ramshaw et al. teaches a fusion polypeptide comprising a first amino acid sequence that can bind to a carbohydrate on a glycoprotein, and a second amino acid sequence that is a ligand for a cell surface polypeptide, particularly a cytokine receptor. The Office Action further asserts that the first amino acid sequence is the hemagglutinin protein. Applicants disagree and traverse the rejection.

Ramshaw et al. does not teach a nucleic acid encoding a fusion protein. In fact, Ramshaw et al. does not teach a fusion polypeptide at all. Although this reference teaches nucleic acid constructs that encode multiple amino acid sequences, they are expressed as separate molecules, rather than as a fusion polypeptide. This is expressly evident from the drawings of Ramshaw et al., especially Figure 6a. Moreover, Ramshaw's specification clearly states at column 7, lines 6-8, that the hemagglutinin and cytokine were coexpressed from the viral constructs, but from separate sites in the viral genome. Thus, they are not combined in a fusion polypeptide.

In order to support a rejection under §102, a reference must teach all elements of the claimed invention. Since a fusion polypeptide is a recited element of the claimed invention, and since Ramshaw et al. fails to teach a fusion polypeptide, the Ramshaw et al. does not anticipate the instant invention. Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

**Rejection of Claims 13-14, 67-68, 86-87, and 140-141 Under 35 U.S.C. §103(a)**

The Office Action rejects claims 13-14, 67-68, 86-87, and 140-141 as being obvious over Ramshaw et al. Specifically, the Office Action states that it would have been obvious to extend the teachings of Ramshaw et al. to other influenza subtypes. The Office Action further states that "the fusion polypeptide of Ramshaw does not comprise a linker", but that it would have been obvious to include one "to optimize the activity of the fusion polypeptide". Applicants disagree and traverse the rejection.

In referring to Ramshaw et al. under 35 U.S.C. §103, the Office Action cites "the fusion polypeptide of Ramshaw et al". However, as Applicants discuss above, Ramshaw et al. does not teach a fusion polypeptide, a recited element of the instant invention, at all. Accordingly, even if modified to include a linker polypeptide, the teachings of Ramshaw et al. still do not teach a fusion polypeptide. Because the prior art, even if modified as suggested by the Office Action does not teach each element of the claimed invention, the instant claims are not obvious over the cited prior art.

Furthermore, Ramshaw et al. offers no motivation to produce a fusion polypeptide, since Ramshaw et al. teaches that coexpression of separate, non-fused proteins from a single expression vector provides effective colocalization.

Indeed, one of ordinary skill in the art would not expect a fusion construct to accomplish the purpose of Ramshaw et al. Hemagglutinin binds efficiently to the carbohydrate sialic acid, which is present on the surface of most mammalian cells. Thus, a fusion polypeptide comprising a sialic acid binding moiety, e.g. hemagglutinin, would adsorb indiscriminately to cells at the site of expression. This would be expected to restrict the fusion polypeptides from reaching the specific immune cells that express receptors for the cytokine moiety of the putative fusion protein (which, again, Ramshaw et al. do not actually teach at all). One of skill in the art would also reasonably expect that, even if one of the fusion protein molecules were to contact a cytokine-responsive cell, the simultaneous binding to sialic acid might interfere with the cytokine receptor mediated events.

It is well settled that the proposed modification to reach a finding of obviousness cannot render the prior art unsatisfactory for its intended purpose; if the modification would render the prior art unsatisfactory for its intended purpose, there can be no suggestion or motivation to make the proposed modification. MPEP §2143.01(V). In addition, if the proposed modification or combination of the prior art would change the principle of operation of the prior art being modified, then the teachings of the references are not sufficient to render the claims obvious. MPEP §2140.01(VI). As described in the preceding paragraph, the proposed modification of Ramshaw et al. stated in the Office Action would require an alteration of the fundamental biological basis of the teachings of Ramshaw et al. Accordingly, the instant claims are not obvious in view of Ramshaw et al., and Applicants request that the rejection be reconsidered and withdrawn.

The Office Action also rejects claims 1-3, 5, 15-22, 24-25, 27, and 67-76, 78, 88-95, 97-98, 100, and 140-147 as being obvious over Hoo et al., U.S. Pat. No. 5,891,432. The Office Action states that Hoo et al teaches a fusion polypeptide comprising a ligand for a cytokine receptor, and further comprising a carbohydrate-

binding domain of a C-type lectin, i.e. P-selectin, as a heterologous membrane attachment domain. According to the Office Action, this alleged teaching renders the instant claims obvious. Applicants disagree and traverse the rejection.

In fact, Hoo et al. does not suggest the use of any carbohydrate-binding domain at all. The 24-amino acid sequence taught by Hoo et al for P-selectin in Table 2 is the transmembrane sequence of P-selectin, and not a carbohydrate-binding domain. Indeed, Hoo et al. use the term "membrane attachment domain" to mean exclusively a sequence that spans at least part of the cell membrane and anchors a polypeptide in the membrane, rather than one that binds to a glycoprotein on the cell surface (see columns 7 and 8, especially column 7, lines 9-12). See also Figure 2 of Johnston et al. *J Biol Chem* 265 : 21381 (1990), showing that the transmembrane sequence is distant from the lectin domain in P-selectin, and Genbank Acc. No. NM 003005, which cites Johnston et al, *ibid*. Furthermore, Hoo et al. aim solely to create chimeric integral membrane proteins, in contrast to the instant invention. Hoo et al. also provides no motivation to include a carbohydrate-binding domain along with the transmembrane domain. Accordingly, Applicants submit that the teachings of Hoo et al. do not render the instant claims obvious, and request that the rejection be reconsidered and withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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